Coagulase-negative staphylococci and endocarditis: reappraisal in the 21st century

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Coagulase-negative staphylococci (CoNS) are a leading cause of nosocomial bloodstream infection[1,2]. Most of these infections are related to intravascular devices and are easily cured with prompt removal of the offending device. Except for prosthetic valve endocarditis (PVE) in which valvular prosthesis-related complications are common[3,4], most cases of CoNS catheter-related infections are uncomplicated, and in sharp contrast to *S. aureus* bloodstream infections[5,6], are uncommonly associated with septic shock or metastasis to distant sites. Because of the benign clinical presentation of most CoNS bloodstream infections and the inability to cure them without prosthesis removal, these infections are often considered a nuisance rather than a serious, life-threatening condition.

The study published in this issue of *Enfermedades Infecciosas y Microbiología Clínica,* "Left-sided native valve endocarditis by coagulase-negative staphylococci: an emerging disease" (*Endocarditis en válvulas nativas izquierdas por estafilococos coagulasa negativos: una entidad en alza*), and other recent studies of CoNS native valve endocarditis (NVE)[3,7-9] alter the paradigm of how clinicians should think of CoNS bloodstream infections. While CoNS NVE was once considered a rare disease, as suggested by recent studies, nosocomial acquisition and an increasing prevalence make this disease worthy of serious consideration in the clinical setting.

Early studies of CoNS NVE indicated that CoNS caused 1% to 3% of cases of NVE[10]. Since then, more recent studies suggest that the prevalence has increased. The current investigation by Haro et al[11] showed that 8.3% of all cases of left-sided NVE were cause by CoNS. This is in agreement with a recent prospective multi-center international cohort study of endocarditis which similarly demonstrated a prevalence of 8%[9]. The temporal nature of this increasing prevalence was demonstrated in this current Spanish study (6.4% prevalence in 1984-1994 to 9.1% in 1995-2005) as well as in an earlier study from England and France[7]. Together, these studies demonstrate that the increasing use of intravascular devices and invasive procedures in the contemporary era has not been without consequence.

The important role that invasive devices and procedures play in the emergence of CoNS NVE is highlighted by the high rate of nosocomial acquisition noted in this study and others[4,8,9]. Noteworthy sources that Haro et al identified include hemodialysis, peripheral catheters, and central intravascular catheters, as well as invasive procedures such as cardiac catheterization and prostate surgery. It is not surprising that the affected patient population is the elderly and those with comorbid illnesses. Thus, this study and others call attention to the clinical scenarios that are associated with this disease.

This study is the first to show that the majority (63%) of patients with CoNS NVE had a vegetation size of < 1 cm. Vegetations this small are often detected only by transesophageal echocardiography and can be missed by transthoracic echocardiography[12]. This, in addition to the typically subacute clinical presentation of CoNS bloodstream infections, illustrates how CoNS NVE can be missed early in the course of disease. Thus a high degree of suspicion for CoNS NVE in the appropriate clinical setting is important and could potentially have an impact on patient outcomes.

The poor outcomes reported in this study are similar to those reported in other studies of CoNS NVE[3,8,9]. Over one-half of patients suffered from congestive heart failure and approximately 1 in 4 patients died in the hospital. Interestingly, in this study by Haro et al, mortality was higher among patients whose symptoms evolved over fewer than 21 days (on univariate analysis). As suggested by the authors, these patients were likely diagnosed in the hospital setting or under close observation in outpatient clinical settings. Possible explanations for the higher mortality are a sicker patient population or perhaps a more virulent staphylococcal strain acquired in the hospital setting. Although it is impossible to determine based on the current data, the poor outcomes with CoNS NVE are likely due to a combination of host susceptibility and staphylococcal pathogenicity factors.

The epidemiology of NVE has changed dramatically over the past few decades. Once predominated by viridans streptococci in the community setting, this disease is increasingly becoming a nosocomial infection due to *S. aureus*, with CoNS increasing in prevalence[7,9]. While simple catheter-related CoNS bloodstream infections are common and usually benign, CoNS NVE can be associated with surprisingly poor outcomes. Future efforts should focus on the pathogenesis and prevention of serious CoNS infections.

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